NATIONAL MARROW DONOR PROGRAM®

Entrusted to operate the C.W. Bill Young Cell Transplantation Program,
including Be The Match Registry℠

August 25, 2010

LCDR Sheri Parker
Office of Naval Research (ONR 342)
875 N. Randolph St.
Arlington, VA 22203-1995

Subject: **Quarterly Performance/Technical Report of the National Marrow Donor Program®**

Reference: Grant Award #N00014-08-1-1207 between the Office of Naval Research and the National Marrow Donor Program

Dear Cdr. Montcalm-Smith:

Enclosed is subject document which provides the performance activity for each statement of work task item of the above reference for the period of March 1, 2010 to June 30, 2010.

Should you have any questions as to the scientific content of the tasks and the performance activity of this progress report, you may contact our Chief Medical Officer – Dennis L Confer, MD directly at 612-362-3425.

With this submittal of the quarterly progress report, the National Marrow Donor Program has satisfied the reporting requirements of the above reference for quarterly documentation. Other such quarterly documentation has been previously submitted under separate cover.

Please direct any questions pertaining to the cooperative agreement to my attention (612-362-3403 or at cabler@nmdp.org).

Sincerely,

Carla Abler-Erickson, MA
Sr. Contracts Representative

Enclosure: Quarterly Report with SF298

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14. ABSTRACT

1. Contingency Prepardness: Collect information from transplant centers, build awareness of the Transplant Center Contingency Planning Committee and educate the transplant community about the critical importance of establishing a nationwide contingency response plan.

2. Rapid Identification of Matched Donors : Increase operational efficiencies that accelerate the search process and increase patient access are key to preparedness in a contingency event.

3. Immunogenetic Studies: Increase understanding of the immunologic factors important in HSC transplantation.

4. Clinical Research in Transplantation: Create a platform that facilitates multicenter collaboration and data management.

15. SUBJECT TERMS
Research in HLA Typing, Hematopoietic Stem Cell Transplantation and Clinical Studies to Improve Outcomes

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NATIONAL MARROW DONOR PROGRAM®

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Grant Award N00014-08-1-1207

QUARTERLY
PERFORMANCE / TECHNICAL REPORT
FOR
APRIL 01, 2010 to JUNE 30, 2010
PERIOD 7

Office of Naval Research

And

The National Marrow Donor Program
3001 Broadway Street N.E.
Minneapolis, MN 55413
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QUARTER PROGRESS REPORT

Development of Medical Technology for Contingency Response to Marrow Toxic Agents

April 01, 2010 through June 30, 2010

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IIA. Contingency Preparedness – Objective 1: Recovery of casualties with significant myelosuppression following radiation or chemical exposure is optimal when care plans are designed and implemented by transplant physicians	
IIA.1 Task 1: Secure Interest of Transplant Physicians	**Period 7 Activity:** • Training of RITN center staff at the Radiation Emergency Assistance Center/Training Site (REAC/TS) in Oakridge, TN • 26 RITN center staff members attended REAC/TS Advanced Radiation Medical Emergency training on March 29 & 30, 2010; course lessons included: o Basic Health Physics & Radiation Protection: Part I o A History of Serious Radiological Incidents: The Real Risk o Health Physics & Contamination Control: Part II o Radiation Detection, Monitoring & Protection Laboratory Exercise & Quiz o Diagnosis & Management of the Acute Radiation Syndrome (ARS) o Diagnosis & Management of Internal Contamination o Diagnosis & Management of Acute Local Radiation Injury & Case Review: Yanango Peru o Radiation Sources & Radiological Terrorism o Radiation Emergency Area Protocol Demonstration o Radiation Emergency Medical Management Drill o Radiation Dose Estimations – Problem Solving Session
IIA.1 Task 2: GCSF in Radiation Exposure	**Period 7 Activity:** • No activity this period.

IIA.1 Task 3: Patient Assessment Guidelines and System Enhancements	**Period 7 Activity:** Donor Management tool application efforts were focused on required features and enhancements for the Navy Contingency project. The tool provides the ability to electronically contact the donors via email and allow them to update their contact information and complete an online Health History Questionnaire (HHQ) from the Do It Yourself donor online platform. Information provided by the donor is securely transferred to the donor's record in the tool used to manage Donor Activity; facilitating reporting, storage and review of this information in established donor management systems. Project Outcomes, related to the new versions of the tools used to manage Donor Activity, continue to show favorable results and strong user feedback: • Donors continue to be responsive to online tools. New Online Health History Questionnaire functionality resulted in: (between 10/1/09 – 6/30/10) o 4948 "Completed" HHQs o 239 "In Process" HHQs • Overall time Savings. o 1,113 hours saved for completed HHQs o 50% reduction in processing time per Online HHQ **Navy Contingency Project Pilot Release 2** Work continues on creating an Event Portal Workflow Management Application to manage contingency events, *initially for preliminary search event.* Key features included in this Release: • Ability to track preliminary event donors in a central screen, for purposes of donor management. • Ability to import the preliminary event donors, as identified through the preliminary event daily report. • Ability to export the preliminary event donors for purpose of supporting address validations, manual

	mail merges or automated letter merges. Key statistics gathered to date for the 4 donor centers in the pilot: • 426 emails requests sent to donors requesting a completed preliminary search HHQ • 620 HHQs completed • 211 preliminary search donors activated • 6 day average close date on an HHQ The General Release of Event Portal is scheduled for end of July 2010, and will be available to all domestic NMDP Network donor centers, excluding the DoD, DKMS Americas, Gift of Life Registry and Caitlyn Raymond Registry. Overall feedback and processing metrics will be monitored and reported. Adding the Event Portal Workflow Management functionality will continue to add to the productivity gains of donors screened using this method. It is expected that NMDP will gain: • The capability to double the capacity to process an HHQ using the same number of staff resources. • The ability to scale for a contingency event requiring confirmation of the availability and suitability of a large number of donors.
IIA.1 Task 4: National Data Collection Model	**Period 7 Activity:** • No activity this period.
IIA. Contingency Preparedness – Objective 2: Coordination of the care of casualties who will require hematopoietic support will be essential in a contingency situation.	
IIA.2 Task 1: Contingency Response Network	**Period 7 Activity:** • Activities of RITN Medical Advisor included: o Drafting of 2010 RITN two year strategic plan o Meetings with DHHS-ASPR staff o Conference calls with RITN Executive Committee o Conference call with National Security Council staff o Review and update of RITN ARS Treatment Guidelines

	• NMDP staff attended the Wake Forest, NC on May 5, 2010 to observe and provide support as requested to RITN center staff as they conducted their 2010 RITN Tabletop Exercise
IIA.2 Task 2: Sibling Typing Standard Operating Procedures	**Period 7 Activity:** • No activity this period.
IIA. Contingency Preparedness – Objective 3: NMDP's critical information technology infrastructure must remain operational during contingency situations that directly affect the Coordinating Center.	
IIA.3 Task 1: I.S. Disaster Recovery	**Period 7 Activity:** Disaster Recovery (DR): • Completed assessment to "true up" existing or missing infrastructure and software, validated need to work with application development teams to build DR infrastructure to support changes to external and internal production applications • Purchased and implemented NetApps Storage devices (i.e., NetApps 6080 clustered storage and 2040 storage devices) to support Snap Shots between our Production and Disaster Recovery sites. This work is a major improvement to our site-to-site recovery processes and will facilitate our upcoming Disaster Recovery Test.
IIA.3 Task 2: Critical Facility and Staff Related Functions	**Period 7 Activity:** • Site visits were conducted at the NMDP operated donor centers in Charlotte, NC (May 4, 2010) and Cleveland, OH (June 23, 2010) o At these site visits the Business Continuity Planner reviews the Business Continuity Action Guide with staff to better prepare each location for responding to incidents that interrupt operations ranging from power or Internet outages to severe weather. • Coordinated the plans for installation of high tinsel strength security film on the windows of the NMDP Repository services building

IIB. Rapid Identification of Matched Donors – Objective 1: Increasing the resolution and quality of the HLA testing of volunteers on the registry will speed donor selection.	
IIB.1 Task 1: Increase Registry Diversity	**Period 7 Activity:** • No activity this period.
IIB.1 Task 2: Evaluate HLA-DRB1 High Res typing	**Period 7 Activity:** • This task is closed.
IIB.1 Task 3: Evaluate HLA-C Typing of Donors	**Period 7 Activity:** • This task is closed.
IIB.1 Task 4: Evaluate Buccal Swabs	**Period 7 Activity:** • No activity this period.
IIB.1 Task 5: Enhancing HLA Data for Selected Donors	**Period 7 Activity:** • No activity this period.
IIB.1 Task 6: Maintain a Quality Control Program	**Period 7 Activity:** • No activity this period.
IIB. Rapid Identification of Matched Donors – Objective 2: Primary DNA typing data can be used within the registry to improve the quality and resolution of volunteer donor HLA assignments.	
IIB.2 Task 1: Collection of Primary Data	**Period 7 Activity:** • Continued working on designing real-time interpretation of all types of incoming primary data.

IIB.2 Task 2: Validation of Logic of Primary Data	**Period 7 Activity:** • This task is closed.
IIB.2 Task 3: Reinterpretation of Primary Data	**Period 7 Activity:** • This task is closed.
IIB.2 Task 4: Genotype Lists & Matching Algorithm	**Period 7 Activity:** • Completed writing and testing SBT interpretation code. Able to interpret all the samples from test messages from Histogenetics and Labcorp • Started working on operationalizing the code in order to interpret all incoming SBT typings in real-time.
IIB. Rapid Identification of Matched Donors – Objective 3: Registry data on HLA allele and haplotype frequencies and on the nuances of HLA typing can be used to design computer algorithms to predict the best matched donor.	
IIB.3 Task 1: Phase I of EM Haplotype Logic	**Period 7 Activity:** • Business systems analyst wrote detailed technical requirements for HapLogic Phase III. • Created a series of HapLogic algorithm process diagrams in order to understand the steps and technical decisions made by the algorithm in Phase II, and what changes will be needed in Phase III. • Created detailed business and system requirements for HapLogic Phase III.
IIB.3 Task 2: Enhancement of EM Algorithm	**Period 7 Activity:** • Presented full-registry high resolution haplotype frequency estimation methods and data at EFI meeting.

IIB.3 Task 3: Optimal Registry Size Analysis	**Period 7 Activity:** • Validated simulation study of cord inventory depletion on the Be The Match registry, that shows enrichment for rare HLA types in large cords remaining after depletion. • Completed study of match rates for CCR5-doubledelta32 cords • Revised study of sources of error in the registry models report to include magnitude and direction of errors. • Found major error in match rate calculation for BMCC benchmark which gave underestimation of match rates and uncovered a mistaken assumption in the registry models report that newly-recruited cords would have a TNC of greater than 90 X 10^7. Both errors have been corrected.
IIB.3 Task 4: Target Under- Repre-sented Phenotypes	**Period 7 Activity:** • Started building a comprehensive database to hold all research data in this task (as well as ensuring proper backups). During this period the table structures and ETL code to conform to NMDP Standards were laid out. Additionally the ETL processes were created and unit tested. • Environmental Systems Research Institute (ESRI) was consulted about the process of automating map production for large numbers of HLA files. Progress was made on determining the best technology options to pursue and finding an ESRI program consultant to engage.
IIB.3 Task 5: Bioinformatics Web Site	**Period 7 Activity:** • This task is closed.
IIB.3 Task 6: Consultants to Improve Algorithm	**Period 7 Activity:** • This task is closed.
IIB.3 Task 7: Population Genetics	**Period 7 Activity:** • No activity this period.

IIB.3 Task 8: Haplotype Matching	**Period 7 Activity:** • No activity this period.
IIB.3 Task 9: Global Haplotype/Benchmark	**Period 7 Activity:** • No activity this period.
IIB. Rapid Identification of Matched Donors – Objective 4: Reducing the time and effort required to identify closely matched donors for patients in urgent need of HSC transplants will improve access to transplantation and patient survival in the context of a contingency response and routine patient care.	
IIB.4 Task 1: Expand Network Communications	**Period 7 Activity:** • No activity this period.
IIB.4 Task 2: Central Contingency Management	**Period 7 Activity:** Donor testing continued for a research project to validate the "actual" HLA-A, B, C and DRB1(8/8) high resolution match rates for both CAU and AFA patients and supply valuable information regarding donor selection in the event of a contingency. Donors were tested in rounds of priority for cost efficiency. Final testing for the CAU and AFA groups 8/8 match rate continues. Testing these groups for the 7/8 match rate was also initiated. An abstract summarizing the data to date was submitted and accepted for poster presentation at the 2010 ASHI annual meeting. A group of 200 Hispanic and 200 Asian/Pacific Islander pseudo patients were selected to estimate the match rates in those race groups. 1033 donors were tested and results compiled for the analysis. Testing will continue into the next quarter.
IIB.4 Task 3: Benchmarking Analysis	**Period 7 Activity:** • This task is closed.

IIB.4 Task 4: Expand Capabilities of Collection and Apheresis Centers	**Period 7 Activity:** • This task is closed.
IIC. Immunogenetic Studies – Objective 1: HLA mismatches may differ in their impact on transplant outcome, therefore, it is important to identify and quantify the influence of specific HLA mismatches. In contingency situations it will not be possible to delay transplant until a perfectly matched donor can be found.	
IIC.1 Task 1: Donor Recipient Pair Project	**Period 7 Activity:** In 1994 a retrospective D/R Pair HLA typing project to characterize class I and class II alleles of donor/recipient paired samples from NMDP's Repository was initiated. The goals of this ongoing research project are to assay the impact of DNA-based HLA matching on unrelated donor transplant outcome, develop strategies for optimal HLA matching, evaluate the impact of matching at alternative HLA loci on transplant outcome and finally to promote the development of DNA-based high resolution HLA typing methodologies. • Audit analysis of SG 25 was completed. • 96% of SG 25 pairs (period of performance closed April 30, 2010) have been audited and are available for inclusion in research studies. • The additional 820 samples typed at DPB1 in SG 25 to support an IBWC study of HLA mismatching in non-malignant disease were completed.
IIC. Immunogenetic Studies – Objective 2: Even when patient and donor are HLA matched, GVHD occurs so other loci may play a role.	
IIC.2 Task 1: Analysis of non-HLA loci	**Period 7 Activity:** The Immunobiology Project Results (IPR) database and its applications will allow for storage and analysis of all immunogenetic data collected on NMDP research samples. This database will replace the existing HLA donor/recipient pair's database and facilitate storage and analysis of data from other immunogenetic loci (KIR, microsatellites, single nucleotide polymorphisms, etc). • IPR Version 1.0, which accepts, validates, and stores incoming HLA and KIR typing data via HML,

	& has comparison, reports, manual override and discrepancy tools was released, along with the application which loads transplant center typings and recreates requests for lab typings. A few deficiencies were noted by the business. • IPR Version 1.1 was released which corrected the deficiencies from Release 1.0. • Quality assurance and corrections were done on an application which loads transplant center typings. • Quality assurance and UAT were completed on software tools that monitor and resolve typing discrepancies. • IPR Version 2.0 which will include functionality such as the Audit tool and Audit report was planned.
IIC.2 Task 2: Related Pairs Research Repository	**Period 7 Activity:** • No activity this period.
IIC. 2 Task 3: CIBMTR Integration	**Period 7 Activity:** • No activity this period.
IID. Clinical Research in Transplantation – Objective 1: Clinical research in transplantation improves transplant outcomes and supports preparedness for a contingency response.	
IID.1 Task 1: Observational Research, Clinical Trials and NIH Transplant Center	**Period 7 Activity:** **Observational Research** • Staff continued work on various observational studies within the area of Immunobiology, GVHD and Graft Sources Working Committees. Two manuscripts were published during this reporting period. **Prospective Studies; RCI BMT** • During this report period, follow up activities continued for donors participating in the PBSC vs. Marrow clinical trial. Staff continues to support this activity including monitoring.

	• Adult Double Cord trial activity during this period included four patients being enrolled for a total of thirty six patients accrued to this study, giving us a 65% completion rate. Staff continues to coordinate and complete monthly PI and coordinator calls, manage data collection and monitor sites. • Revlemid trial activity continued during this period. Sites continued to enroll patients onto this study using the EMMES developed data capture forms. Minor revisions to the data capture system have been identified and have or are currently being revised. • The survey research team continues to develop processes and add staff to support studies requiring their expertise.
IID.1Task 2: Research with NMDP Donors	**Period 7 Activity:** • Staff continued support of a Donor Ethnicity study with Dr. Galen Switzer from the University of Pittsburgh. • Staff continued to collaborate on a COG KIR study. Activities include facilitating the collection of a donor blood sample and shipment to the study lab. • Staff continued to work on identifying and streamlining the operational processes needed to implement the protocol for long-term donor follow-up.
IID.1 Task 3: Expand Immuno-biology Research	**Period 7 Activity:** • No activity this period.

ACRONYM LIST

AABB	American Association of Blood Banks	IBWC	Immunobiology Working Committee
AFA	African American	IDM	Infectious Disease Markers
AGNIS	A Growable Network Information System	IHWG	International Histocompatibility Working Group
AML	Acute Myelogenous Leukemia	IPR	Immunobiology Project Results
ABD	Antigen Binding Domain	ICRHER	International Consortium for Research on Health Effects of Radiation
API	Asian Pacific Islander	IND	Investigational New Drug
ARS	Acute Radiation Syndrome (also known as Acute Radiation Sickness)	IS	Information Services
ASBMT	American Society for Blood and Marrow Transplantation	IT	Information Technology
ASHI	American Society for Histocompatibility and Immunogenetics	IRB	Institutional Review Board
B-LCLs	B-Lymphoblastoid Cell Lines	JCAHO	Joint Commission on Accreditation of Healthcare Organizations
BARDA	Biomedical Advanced Research and Development Authority	KIR	Killer Immunoglobulin-like Receptor
BCPeX	Business Continuity Exercise	MDACC	MD Anderson Cancer Center
BBMT	Biology of Blood and Marrow Transplant	MDS	Myelodysplastic Syndrome
BMT	Bone Marrow Transplantation	MHC	Major Histocompatibility Complex
BMT CTN	Blood and Marrow Transplant - Clinical Trials Network	MICA	MHC Class I-Like Molecule, Chain A
BRT	Basic Radiation Training	MICB	MHC Class I-Like Molecule, Chain B
C&A	Certification and Accreditation	MKE	Milwaukee
CAU	Caucasian	MSKCC	Memorial Sloan-Kettering Cancer Center
CBMTG	Canadian Blood and Marrow Transplant Group	MSP	Minneapolis
CBB	Cord Blood Bank	MUD	Matched Unrelated Donor
CBC	Congressional Black Caucus	NCBM	National Conference of Black Mayors
CBS	Canadian Blood Service	NCI	National Cancer Institute
CBU	Cord Blood Unit	NEMO	N-locus Expectation-Maximization using

			Oligonucleotide typing data
CHTC	Certified Hematopoeitic Transplant Coordinator	NHLBI	National Heart Lung and Blood Institute
CIBMTR	Center for International Blood & Marrow Transplant Research	NIH	National Institutes of Health
CIT	CIBMTR Information Technology	NIMS	National Incident Management System
CLIA	Clinical Laboratory Improvement Amendment	NK	Natural Killer
CME	Continuing Medical Education	NLE	National Level Exercise
CMF	Community Matching Funds	NMDP	National Marrow Donor Program
COG	Children's Oncology Group	NRP	National Response Plan
CREG	Cross Reactive Groups	NST	Non-myeloablative Allogeneic Stem Cell Transplantation
CSS	Center Support Services	OCR/ICR	Optical Character Recognition/Intelligent Character Recognition
CT	Confirmatory Testing	OIT	Office of Information Technology
CTA	Clinical Trial Application	OMB	Office of Management and Budget
DC	Donor Center	ONR	Office of Naval Research
DHHS-ASPR	Department of Health and Human Service – Assistant Secretary Preparedness and Response	P2P	Peer-to-Peer
DIY	Do it yourself	PBMC	Peripheral Blood Mononuclear Cells
DKMS	Deutsche Knochenmarkspenderdatei	PBSC	Peripheral Blood Stem Cell
DMSO	Dimethylsulphoxide	PCR	Polymerase Chain Reaction
DoD	Department of Defense	PSA	Public Service Announcement
DNA	Deoxyribonucleic Acid	QC	Quality control
D/R	Donor/Recipient	RCC	Renal Cell Carcinoma
EBMT	European Group for Blood and Marrow Transplantation	RCI BMT	Resource for Clinical Investigations in Blood and Marrow Transplantation
EM	Expectation Maximization	REAC/TS	Radiation Emergency Assistance Center/Training Site
EMDIS	European Marrow Donor Information System	RFP	Request for Proposal
ENS	Emergency Notification System	RFQ	Request for Quotation
ERSI	Environment Remote Sensing Institute	RG	Recruitment Group
FBI	Federal Bureau of Investigation	RITN	Radiation Injury Treatment Network

FDA	Food and Drug Administration	SBT	Sequence Based Typing
FDR	Fund Drive Request	SCTOD	Stem Cell Therapeutics Outcome Database
Fst	Fixation Index	SG	Sample Group
GETS	Government Emergency Telecommunications Service	SLW	STAR Link® Web
GCSF	Granulocyte-Colony Stimulating Factor (also known as filgrastim)	SSA	Search Strategy Advice
GIS	Geographic Information System	SSO	Sequence Specific Oligonucleotides
GvHD	Graft vs Host Disease	SSP	Sequence Specific Primers
HCT	Hematopoietic Cell Transplantation	SSOP	Sequence Specific Oligonucleotide Probes
HEPP	Hospital Emergency Preparedness Program	STAR®	Search, Tracking and Registry
HHQ	Health History Questionnaire	TC	Transplant Center
HHS	Health and Human Services	TED	Transplant Essential Data
HIPAA	Health Insurance Portability and Accountability Act	TNC	Total Nucleated Cell
HIS	Hispanic	TSA	Transportation Security Agency
HLA	Human Leukocyte Antigen	UI	User Interface
HML	Histoimmunogenetics Mark-up Language	URD	Unrelated Donor
HR	High Resolution	WGA	Whole Genome Amplification
HRSA	Health Resources and Services Administration	WMDA	World Marrow Donor Association
HSC	Hematopoietic Stem Cell	WU	Work-up